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(1) INTRODUCTION: Narrative that briefly (one paragraph) describes the subject, purpose, and scope of the research.

The goal of this research is to use high spectral and spatial resolution (HiSS) MR imaging to improve images of human and murine prostate. Our work on the application of HiSS to improve anatomic and functional imaging was first described in a paper in Academic Radiology [1]. Related work from this laboratory is presented in a number of other publications [2-9]. Work from other laboratories shows that closely related methods also provide advantages for anatomic [10] and functional [11-14] MRI.

This significant body of work provides support for the feasibility of ongoing experiments in this laboratory. Specifically, we expect to 1) improve separation of water and fat signals 2) increase image contrast 3) increase sensitivity to contrast agents and to local physiology – and as a result improve detection of suspicious lesions such as cancers and particularly delineation of tumor edges. We expect that this will increase the sensitivity and specificity of MR scans for prostate cancer. To achieve these goals our original 'statement of work' is summarized as follows:

A. Develop high spectral and spatial resolution (HiSS) magnetic resonance imaging (MRI): We will implement fast, high-resolution, high-spectral bandwidth imaging on a 4.7 Tesla (T) scanner. The 4.7 Tesla scanner will be upgraded with a next-generation control console during the next six months. K-space trajectories of HiSS pulse sequences will be corrected for eddy-current effects. Spectral data will be processed to obtain pure absorption spectra in which truncation artifacts are minimized in each voxel. Images will be synthesized in which intensity is proportional to water resonance peak height, line width, integral, resonance frequency, number of resolved components of the water signal, and other features of the water and fat signals. To test whether the methods are working properly we will image phantoms that are constructed to provide complicated structures with differing susceptibility. In addition, we will test the methods by imaging rat brains – the brain, unlike tumor tissue, has a precisely defined and well-characterized anatomy.

B. CAD (computer-aided diagnosis) techniques developed by Dr. Jiang and colleagues will be adapted for use with HiSS MRI datasets. The texture of images derived from HiSS datasets, i.e., the spatial variation in image intensity, will be measured quantitatively. Tumor edges will be analyzed to determine their degree of irregularity. Changes in HiSS data following contrast media injection will be measured. These methods will be developed iteratively and in parallel with MR studies of metastatic and non-metastatic rodent tumors (see below). Each new version of the CAD method will be evaluated based on its ability to discriminate between metastatic and non-metastatic tumors.

C. Evaluation of HiSS MRI and use of HiSS MRI to compare metastatic and non-metastatic rodent tumors implanted in murine hind limb and in murine prostate.

D. Studies of human prostate cancer: We will evaluate the accuracy of HiSS imaging of patients with prostate abnormalities.

(3) BODY:

SOW A. We implemented several different versions of HiSS on our 4.7 Tesla scanner including gradient echo echo-planar spectroscopic imaging and spin echo echo-planar spectroscopic imaging using both sinusoidal and trapezoidal gradients to sample k-space. HiSS MRI images obtained using EPSI were compared to conventional spin echo and gradient echo imaging and conventional spectroscopic imaging. In many cases HiSS showed improved detail compared to conventional imaging and in particular delineated tumors and blood vessels associated with tumors more clearly. HiSS data acquired using EPSI were very similar to HiSS data acquired using conventional SI - suggesting the eddy current effects were not significant. We acquired data from both metastatic and non-metastatic tumors implanted orthotopically and in the hind-limb.

SOW B: With Dr. Yulei Jiang, we are developing CAD methods for analyzing contrast enhanced MRI data. An abstract by Yahui Peng describing this work has been submitted to the RSNA. Application of neural network methods allowed improved differentiation of metastatic and non-metastatic rodent prostate tumors.

SOW C: We do not yet have sufficient data to perform a statistically valid comparison of metastatic and non-metastatic cancers.

SOW D: Studies of human cancer: We have implemented high resolution EPSI with our pelvic array coil on two of the clinical scanners. We have tested it in phantoms and have performed a number of scans of prostates of volunteers and these scans show interesting and potentially useful contrast that is not available in conventional images. We have not yet begun to scan patients because our institution is negotiating with the DOD regarding some provisions of the consent form. We hope an agreement will be reached in the next month or two. Then we will amend our IRB protocol accordingly and proceed with patient scans.

4) KEY RESEARCH ACCOMPLISHMENTS: Bulleted list of **key** research accomplishments emanating from this research

- We demonstrated advantages of HiSS imaging of orthotopic prostate cancer in mouse and we are preparing an abstract and paper describing this work.
- We demonstrated advantages of HiSS imaging of prostate tumors implanted in murine hind limb and imaged contrast media uptake in these tumors.
- Developed a protocol incorporating HiSS imaging into routine scans of human prostate.
- Developed a new approach to improving contrast in MR images based on analysis of the Fourier components of inhomogeneously broadened resonances.
- We developed new approaches to suppressing noise and accurately reconstructing EPSI image data.
- Begun to develop CAD methods for MRI data

(5) REPORTABLE OUTCOMES:

a. Karczmar GS, Fan X, Al-Hallaq HA, River JN, Tarlo K, Kellar K, Zamora M, Rinker-Schaeffer C, and Lipton MJ. Functional and anatomic imaging of tumor vasculature: High-resolution MR spectroscopic imaging combined with a superparamagnetic contrast agent. Academic Radiology **9***:* S352-4, 2002.

b. Fan X, Du W, Zamora M, MacEneaney PM, and Karczmar GS. "Structure of the water resonance in small voxels in rat brain detected with high spectral and spatial resolution MRI," in press, Journal of Magnetic Resonance Imaging **16**: 547 - 552 2002.

c. Du W, Karczmar G, Pan X. "Effects of constant frequency noise in magnetic resonance imaging with non-uniform sampling", Journal of Medical Physics, Med Phys **29**:1832-1838, 2002.

d. Du W, Du Y, Fan X, Zamora M, Karczmar G. "Reduction in Spectral Ghost Artifacts in high resolution EPSI using post processing algorithms", Magnetic Resonance in Medicine, *in press*.

– Degrees obtained that were/are supported by this award;

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(6) CONCLUSIONS: Our results to date demonstrate quantitatively that there are significant advantages associated with high spectral and spatial resolution imaging of the prostate. During the next year we will begin quantitative comparison of HiSS and conventional images in metastatic and non-metastatic murine tumors and continue to improve our methods for data acquisition and analysis. We also expect to receive approval for scanning prostate patients and scan 5 – 10 patients who are scheduled for radical prostatectomy. We will compare the MR images to biopsy results.

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